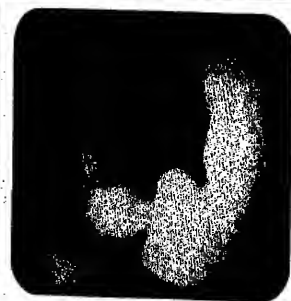


The Upper Functional G.I. Disorder

The Pseudo-ulcer



Ulcer-like symptoms: no G.I. pathology

The patient is convinced it's an ulcer. However, symptoms are quite typical, and x-ray findings are negative. These findings and the results of additional diagnostic procedures exclude an organic basis for the patient's complaints. A diagnosis of "upper functional gastrointestinal disorder" is made, which is supported by the fact that episodes of painful symptoms coincide with episodes of excessive anxiety, as indicated by the history.

It may be useful to explain to the patient the mechanism by which emotions upset normal G.I. functioning, resulting in hypersecretion and hypermotility and thus causing such symptoms as nausea and epigastric pain. In upper functional gastrointestinal disorders, counseling by the primary physician can often help the patient to understand how excessive anxiety may cause flare-ups of G.I. symptoms.

A disproportionate number of patients seen by the general practitioner suffer from functional disorders, as do more than half of those seen by the gastroenterologist.* Where milder cases may respond to counsel-

ing alone, if symptoms are severe and disabling to any degree, a suitable regimen may include medication to reduce the symptoms and the excessive anxiety that often provokes these distressing symptoms. In these cases, Librax as an adjunct can greatly contribute to the course of therapy. Its dual action can offer relief of both painful symptoms and excessive anxiety, because each capsule contains 5 mg chloridazepoxide HCl and 2.5 mg cimetidine Br. The anti-anxiety action of Librax® (chloridazepoxide HCl) makes Librax exceptional

An adjunct
in anxiety-related upper
functional G.I. disorders
Librax®
Each capsule contains 5 mg chloridazepoxide HCl
and 2.5 mg cimetidine Br.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Symptomatic relief of hypersecretion, hypermotility and anxiety and tension states associated with organic or functional gastrointestinal disorders; and as adjunctive therapy in the management of peptic ulcer, gastric duodenal, irritable bowel syndrome, spastic colitis, and mild ulcerative colitis.

Contraindications: Patients with glaucoma; possible hypertrophy and benign bladder neck obstruction; known hypersensitivity to chloridazepoxide hydrochloride and/or cimetidine bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librax (chloridazepoxide hydrochloride) to known addiction-prone individuals or those who might increase dosage without medical supervision (including convalescing patients following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in

pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anti-cholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, drowsiness, or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, carefully consider with other psychotropics seems indicated, carefully consider behavior pharmacologic effects, particularly in use of potent sedating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, agitation and acute rage) have been reported in psychiatric patients. Employ usual precautions in psychiatric states with episodes of impending depression, suicidal tendencies may be present and protective measures necessary. Variable effect on blood coagulation have been reported very rarely. In patients receiving the drug and oral anticoagulants, causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not seen with either component alone have been reported with Librax. When chloridazepoxide hydrochloride is used alone, drowsi-

ness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances, symptoms have been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all in frequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage beta activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis, leukopenia and hemolytic dysfunction) have been reported occasionally with chloridazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anti-cholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

ROCHE Roche Laboratories, Inc., Nutley, New Jersey 07110

ABCD

Medical Tribune

world news of medicine and its progress

making rounds

CHILD SUICIDES—The National Poison Center at Children's Hospital, Pittsburgh is seeing many "accidental poisonings" of 6 to 10-year olds that may be attempted suicides, center director Dr. Richard W. Moriarty told MT. Such children are too young for truly accidental ingestion of medicines or household poisons, and too young for drug abuse. Many are in "intolerable" family situations or have problems at school. M.D., he said, "need to take a little more seriously the fact that indeed kids can have these kinds of problems that can lead them to quite desperate moods."

'It Can't Be Extrapolated'

Belgian Expert Says UGDP Study Is Valid Within Own Context

By JAMES MAHER
Medical Tribune Staff

GENEVA—"The U.G.D.P. study is quite valid within its own context, but it simply cannot be extrapolated to the whole diabetic population," according to Dr. Jean Pirart, secretary of the Belgian Diabetic Association.

Dr. Pirart was among several leading European investigators and clinicians asked by MEDICAL TRIBUNE to comment upon the clinical implications of recent Biometric Society analysis of the University Group Diabetes Program study. The 1970 U.G.D.P. report claimed a higher than expected cardiovascular mortality associated with oral hypoglycemic agents, but no difference in overall mortality.

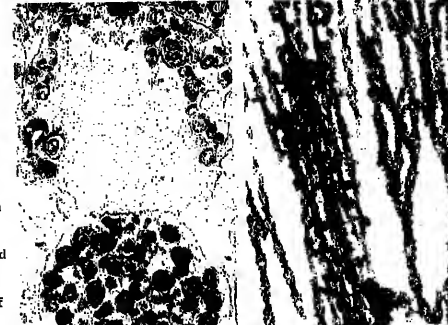
Third of a Series

"In the view of Belgian diabetologists, the hypoglycemics have to be used according to the correct indications, and the correct dosages. If these conditions are met, then we do not consider that there is a high risk of toxicity."

Dr. Pirart said that at present in Belgium the general pattern of diabetic therapy is: insulin—20 per cent; oral drugs, combined with dietary control—about 40 per cent.

Dr. Pirart warned, though, that he

Arteriosclerotic Basis Denied For Bulk of Senile Dementia



"Twisted tubules" characteristic of the neurofibrillary tangle in senile brain, right, may be a pair of helically wound filaments or a periodically constricted tubule. Contents of abnormal neurites making up senile plaque, left, are seen as dense inclusions, degenerating mitochondria, "twisted tubules."

By FRANCIS COCHRAN
Medical Tribune Staff

NEW YORK—What causes senile dementia with the characteristic lesions seen in affected brains?

Contrary to a still-prevalent belief, most cases cannot be attributed to arteriosclerosis, Dr. Robert D. Terry emphasized here during an interview in which he outlined recent research findings on this disorder.

The neuropathologist, who heads the Department of Pathology at Albert Einstein College of Medicine, said that observations on autopsied brains have proved that "relatively few cases of senile dementia are accounted for by atheromatous changes in major arteries."

Instead, Dr. Terry considers the most common type of senile dementia

Prospects Grim For Some States In Liability Mess

By EDWARD GROSSMAN
Medical Tribune Staff

NEW YORK—Will it be a long hot summer on the malpractice front?

Based on nationwide interviews conducted by MEDICAL TRIBUNE with physicians, medical society executives, political leaders, and lawyers, the forecast is for things to stay relatively cool in some states, thanks as much to good luck and good will as good legislation. But in others, it will probably not be possible to avert the collapse of professional liability-coverage systems and widespread interruption of medical services.

Some Points of Consensus

While most of those interviewed called the situation "fluid," "unclear," or "confused"—with local predictions ranging from bleak to guardedly optimistic—some points of consensus emerged.

It was agreed that few states, however fortunate for the time being, would escape having to grapple with the basics of malpractice reform, as stop-gap legislative measures expire and no aroused public and medical profession demand more rational protection and indemnification. No single reform is the answer, it was emphasized, and the package of changes that

Continued on page 4

Dr. Warren Honored at Bunker Hill Ceremonies



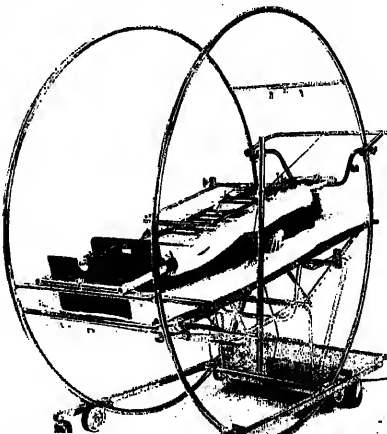
Dr. Joseph Warren dying of his wounds, in John Trumbull's engraving, "Battle of Bunker's Hill."

Bunker Hill. Dr. Warren's revolutionary role was more important than that of better known Paul Revere—whom he sent on at least one of his famous rides.

Colorful, idealistic and democratic,

Continued on page 12

Lung Emboli Held Down in Hip Replacement



After surgery for total hip replacement Dr. Louis Brady recommends patients be placed on the Stryker table bed, shown here. To advance the healing process, his patients were turned to a new position by nurses every eight hours and left at that position as long as they could tolerate it.

Medical Tribune Report

SAN FRANCISCO—Only five of 360 patients who underwent 560 total hip replacements showed evidence of pulmonary embolism and none of the five died—in a prospective study of prophylactic measures described here to the American Academy of Orthopaedic Surgeons.

The use of any of five drugs (dextran, heparin, warfarin, aspirin, and phenylbutazone), while indicated, was combined with standard nursing care measures, including antiembolism hose, calf exercise, and early mobilization, it was reported by Dr. Louis P. Brady, chief of orthopaedics at Florida Hospital, a private hospital not affiliated with any medical school, in Orlando, Fla.

Such a multifaceted approach can reduce significantly the incidence of thromboembolic phenomena, he said. Ninety-five per cent of the 360 patients received dextran 40, and 19 per cent received a combination of dextran and sodium warfarin. Heparin was used only to treat pulmonary embolism.

Meticulous Care Essential

Four patients developed thromboembolism ("as opposed to phlebotrombosis"); 53 developed edema and were "clinically felt" to have phlebotrombosis. All patients with phlebotrombosis developed edema.

"No single parameter will accomplish these results," Dr. Brady cautioned. "Meticulous care and careful observation of the patient by a discerning and interested surgeon is mandatory to [the protocol's] success."

"Delegation of the ultimate responsibility to others is usually not possible. One must develop a protocol which will suit his own situation and then rigidly adhere to it if successful results are to be anticipated."

"Some people think [anti-embolic] hose are a big thing," Dr. Brady told

MEDICAL TRIBUNE, "Some people routinely put their patients on aspirin. What we tried to do was to develop a rational approach using whatever was available that fit the patient."

Chamley and George have cautioned. Dr. Brady noted that a series of total hip replacements could reach 300 to 500 patients with no significant problems, only to be followed by the development of thromboembolic phenomena in six to eight of the next 100 patients.

But he said that patients will be added to this series at the rate of about 150 a year, and there are no plans to change the protocol, "because we think we have a winner."

Departures From Routine

Although Dr. Brady said no part of the protocol should be considered more important than another, he did remark that the two elements that differ most from what is routine in other institutions are the stress laid on the preoperative education of the patients and the use of the Stryker table bed.

The preoperative orientation of the patients was really a training program carried out by nurses who were themselves rigorously trained for the project, Dr. Brady said.

"The patients were frankly told they could be in for a lot of grief in the post-operative period," he said, "and they responded by helping themselves."

The Stryker table bed is hardly used in other institutions for postoperative hip replacement patients, Dr. Brady said, but in this study all 360 patients were placed on the table bed immediately after surgery.

After surgery, patients were immediately placed on the Stryker table bed. They were turned to a new position by nurses every eight hours and left at that position as long as they could tolerate it—usually about an hour. When

supine, they were kept in 20° of Trendelenburg.

Dr. Brady stressed the importance of the role played by the nurses in seeing that the patients followed instructions for active and isometric exercises and the recognition of early edema.

Antiembolism hose were used only when there was evidence of clinical edema, in which case they were applied to both legs below the knee only.

"I feel their routine use increases the likelihood of heel sores," Dr. Brady said, "and prohibits good skin care."

Name of the patients in this study developed heel sores.

If edema worsened on the day after it was discovered, sodium warfarin was given (15 mg. the first day and 10 mg. the second), to maintain the prothrombin time at one and a half to two times control, with daily prothrombin times beginning the third day.

When pulmonary embolism occurred, as it did in five patients, sodium warfarin was discontinued and heparin started. These five were the only patients whose activity was restricted, and then it was only for three to four days, until symptoms subsided.

Patients with thromboembolism were given phenylbutazone (100 mg. t.i.d.), usually for three days or until symptoms subsided.

Stand to Tolerance on 3d Day

All patients were allowed to stand to tolerance in the Stryker table bed beginning on the third day after surgery.

On the sixth day, the patients were transferred from the Stryker bed to a regular hospital bed, retention sutures were removed, and ambulation in parallel bars was begun.

Protected weight bearing was allowed on the sixth day for patients with reconstructive procedures; unprotected weight bearing was allowed for patients with uncomplicated osteoarthritis or rheumatoid arthritis.

Sutures were removed on the 13th day and the patients were discharged on the 14th day on crutches or with walkers, with no medication other than supplemental vitamins and iron.



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Study Supports Link Of Type A Behavior With Heart Disease

Medical Tribune Report

NEW ORLEANS—Can a physician cite scientific evidence to back up a warning to a business executive patient that his hard-driving, competitive, intensely-committed behavior may cause coronary heart disease?

The association has been demonstrated, but skepticism has persisted because of a lack of knowledge as to how psychological factors might relate to the pathological processes involved in coronary disease.

Now Boston University investigators have provided data for the practitioner to use. Dr. Stephen J. Zyzanski presented the findings at the annual meeting of the American Psychosomatic Society.

Artery Blockage Related

The double-blind study at the Boston University Medical Center covered 95 men, most of them in the 45-to-55-year age range, who underwent coronary angiography. Cardiologists reviewed cineangiograms and rated the per cent by which each of the four major arteries of the heart—main left, LAD, circumflex, and right coronary—were blocked by atherosclerotic lesions at their most obstructed points.

Before angiography the patients completed self-administered tests to cover behavior, anxiety, neuroticism, hypochondriasis, and hysteria. The coronary-prone behavior pattern—Type A—was characterized as hard-driving, competitive, impatient, hurried, and intensely committed to vocational goals. Angina intensity was recorded from histories.

It was found that 55 men with 50 per cent or greater arterial obstruction in two or more vessels scored statistically higher on the scales of the activity survey than did 37 patients with lesser obstruction.

Men with at least 50 per cent obstruction in two or more vessels scored significantly higher on anxiety and depression, but were not remarkably higher on hypochondriasis. There was no trend in hysteria scores. The more seriously affected men manifested significantly less symptom denial.

No Angina Association

Angina intensity rating had no significant association with activity survey scores.

"Men with more severe and frequent angina scored much higher on hypochondriasis and on hysteria," Dr. Zyzanski reported, "entirely due to a greater tendency to admit symptoms. These men were also higher on the depression scale."

He said the lack of association between Type A scales and angina intensity "is consistent with the hypothesis that Type A characteristics precede rather than follow from the atherosclerotic process."

Associated with Dr. Zyzanski in the study were Drs. C. David Jenkins, Thomas J. Ryan, Steven H. Lefkowitz and Margaret Everist.

4 Investigators Near Trial In 'Illegal Dissection' Case

By HARRIET PAGE

Medical Tribune Staff

BOSTON—More than a year after their indictment for "illegal dissection" under an 1814 grave-robbing statute, four Boston City Hospital physicians will at last come to trial.

The four, Drs. Leon D. Sabath, Leonard Berman, David Chmies, and Agneta Phillipson, had participated in a study of women about to undergo abortions designed to see if erythromycin and chloquidone reach the fetus in therapeutic concentrations after oral administration to the mother.

Their finding, based on examination of amniotic fluid and fetal tissue and reported in *The New England Journal of Medicine* in June, 1973 (288:1219), was that both agents crossed the placenta and that fetal tissue levels reflect maternal dose levels. The authors concluded that, providing the infecting organism is sensitive, "both antibiotics may be reasonable alternatives to penicillin in the treatment of intrauterine infection."

On May 27, Neil Chuyet, defense attorney for the four, appeared in Suffolk County Superior Court before Judge John J. McNaught to argue motions for discovery of the Commonwealth case and to get the bill of particulars from the prosecutor, Assistant District Attorney Newman A. Flanagan. And on June 24, Mr. Chuyet will argue substantive motions for dismissal.

Medical Tribune Report

SAN DIEGO, CALIF.—All postmenarcheal young women whose mothers took diethylstilbestrol in early pregnancy should be examined for nonmalignant changes in the reproductive tract that could be associated with clear-cell adenocarcinoma of the vagina and cervix, according to Dr. Arthur L. Herbst, assistant visiting surgeon at Massachusetts General Hospital.

In a study of 110 young women whose mothers took diethylstilbestrol or related drugs in pregnancy and 82 whose mothers did not, transverse fibrous ridges in the vagina and cervix were observed in about 20 per cent of the exposed but in none in the controls, Dr. Herbst told an American Cancer Society seminar for science writers here.

Effect on Fetal Development

"While these ridges have no relation to malignancy," he said, "they are evidence that diethylstilbestrol has affected the development of the female genital tract in the fetus. In addition, nonmalignant abnormalities of the lining of the vagina were noted in approximately one-half the exposed, compared to only 1 per cent of the controls."

"Almost all of the exposed subjects had similar tissue changes in the lining of the cervix, in comparison to only one-half of the controls. Biopsies of the abnormal areas of the vagina and cervix showed the presence of benign glandular epithelium (vaginal adenosis and cervical ectropion) and associated inflammatory changes."

It was Assistant D.A. Flanagan who prosecuted—and won—the manslaughter case against Dr. Kenneth C. Edelin last March (MEDICAL TRIBUNE, March 12). Dr. Edelin had been indicted at the same time as the other four B.C.H. physicians for causing the death of a fetus during a legal abortion by hysterotomy in October, 1973.

Because of the disposition of the Edelin case—which shocked both the medical and legal communities—there has been some speculation as to the climate that will prevail in the fetal research case. Many observers felt grimly that the disposition of the Edelin case was simply a barometer of how things would be in future such issues.

Directed Verdict Predicted

But William J. Curran, Professor of Legal Medicine at Harvard Medical School, in answer to a telephone query from MEDICAL TRIBUNE, was far more optimistic.

"I was exactly wrong in my prediction for the Edelin case—that he would be acquitted," said Prof. Curran. "But this time I feel confident, and that this case will get a better showing."

"The great outcry over the verdict in the Edelin case should put this one in better perspective. The prosecutors in the Edelin case were attacked vociferously on both medical and legal grounds. The judge's determination to give no sentence may reflect a responsiveness to this."

Postmenarcheal Checkup of Diethylstilbestrol Babies Is Urged

Medical Tribune Report

Although there was no evidence of malignancy in the group of young women studied by Dr. Herbst, he noted that an earlier worldwide study of 179 women who developed clear-cell adenocarcinoma of the reproductive tract showed that two-thirds were associated with treatment of the mother with diethylstilbestrol, diestronol, hexestrol, or other synthetic estrogens.

He also noted that both the malignant and the nonmalignant changes observed in the two studies occurred only in women whose mothers were on hormone therapy before the 18th week of pregnancy. In addition, the benign glandular changes of vaginal adenosis have been found in almost all cases of vaginal adenocarcinoma where adequate tissue was available for study, he pointed out.

Although as many as 2,000,000 young women in the United States have been exposed to diethylstilbestrol prenatally, Dr. Herbst observed that there are only about 100 cases of cancer definitely associated with this cause in this country.

"Thus, the risk of cancer development in any given diethylstilbestrol-exposed female appears to be small," he concluded.

Survival Rates High

At the same time, he said that survival rates for young women in whom the malignant changes were detected early and who underwent hysterectomy or other surgical procedures, have been high.

Panning Rate Squeeze



Playing his flute to attract a crowd, Dr. Louis Brady invited listeners in San Francisco to take a pamphlet on the malpractice insurance question.

"So," Dr. Curran said, "I'll go out on a limb and predict that in this case there will be a directed verdict in favor of the defendants. The key element in this case, which invokes an ancient statute directed at stealing tissue, is consent, and consent was obtained from each of the mothers."

"It is important," Dr. Herbst commented, "that all [prenatally] exposed females be examined once they begin in menarche, or in any event by the age of 14 years. We do not feel it is reasonable to conduct screening examinations on young females before they have had menstrual periods. However, such examinations should have a thorough examination in the event of vaginal bleeding, staining, or unusual persistent vaginal discharge, to rule out the presence of cancer."

"An adequate examination includes careful palpation and visualization of the vagina and cervix, vaginal cytology, iodine staining, and biopsies of abnormal areas that initially appear red or fail to stain with iodine solution. For those who are trained in its use, the colposcope is useful in providing a magnified view of the vaginal and cervical surfaces, and allowing directed rather than random biopsies of any abnormal areas."

"An adequate examination includes careful palpation and visualization of the vagina and cervix, vaginal cytology, iodine staining, and biopsies of abnormal areas that initially appear red or fail to stain with iodine solution. For those who are trained in its use, the colposcope is useful in providing a magnified view of the vaginal and cervical surfaces, and allowing directed rather than random biopsies of any abnormal areas."

Italians Flock to Medicine

Medical Tribune World Service

ROME—More Italian students are studying medicine than any other subject in the national university system, just in the figures released by the National Institute of Statistics for the 1974-1975 academic year.

With a total of 716,375 full-time students, those enrolled in the faculty of medicine and surgery number 137,748 or 19.2 per cent.

index

CLINICAL NEWS NOTE: "The U.G.D.P. study is quite valid within its own context, but it simply cannot be extrapolated to the whole diabetic population." (Dr. Jean Pirani, see page 1.)

Medicine: pgs. 1, 2, 3, 7, 12, 23
Malpractice problems blooming some places, not in others 1
"Illegal dissection" case near trial 3
M.D.s urged to think of responsibility to whole populations 7
Some families found prone to several types of cancer 23

Surgery: pgs. 2, 3, 6, 8, 12, 18
Lung emboli reduced in hip replacement surgery 2
Renal transplant mortality less than 3 per cent at Paris' Necker Hospital 8
Delgado's 2-way cerebral "pacemaker" cases pain 18

Pediatrics: pgs. 3, 18, 19, 23
Quadriceps surgery in children simplified 18
Aerosol anilines "playing Russian roulette" 19
Female lag in sports performance held unrelated to inherited ability 23

Ob/Gyn: pgs. 3, 12
Postmenarcheal checkup urged for diethylstilbestrol babies 3
Patient role suggested in antitumor drug used in pregnancy 12

Psychiatry: pgs. 1, 2, 9
Senile dementia arteriosclerosis held largely innocent 1
Study backs relation of "Type A" behavior and heart disease 2

feature index

Editorial Capsules 6
Current Opinion 9
Editorials 11
Cartoons 12, 13, 17, 23
Wire Talk 15
One Man...and Medicine 17
Medicine on Stamps 19
Elsewhere 21
Sports Report 23
Immunologic Medicine 23

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Renal Transplant Deaths Held to 3% in Paris

By SUE WYMELENBERG
Special Tribune Correspondent

BOSTON—"A series of small improvements in patient treatment" is enabling the Necker Hospital in Paris to reach good survival figures for kidney transplants, Dr. Jean Honnburger told Medical Tribune in an interview during the week he spent as visiting physician-in-chief at the Peter Bent Brigham hospital here.

Dr. Honnburger, who is chief of nephrology at the Necker, said that at his hospital, the most important factor in attaining better survival rates "besides good clinical follow-up—is a series of tests which permits more exact and more lucid treatment of each patient."

"Patients are no longer dying when

they reject a kidney. In the last two years we have had only a 3 per cent death rate in transplants overall."

Almost one-third of the approximately 350 renal transplants performed yearly in France take place at the Necker, although there are some 25 hospitals throughout the country that also do the procedure.

120 Hemodialysis Centers

Hemodialysis is available to patients at 120 centers, most of which are hospital based. The dialysis centers are connected by a teletype system; if a patient cannot be accommodated by one, the system will locate an available bed at another. Treatment results from each center are computerized and generally available to all hospitals.

As in the United States, there is an acute shortage of transplantable kidneys, not only in France but in all of Europe, Dr. Honnburger noted, adding that he is hopeful that the recently organized inter-European kidney exchange will be effective in making more available.

A problem more difficult to solve, he observed, is the shortage in France of medical teams trained to perform transplants.

"In France we now do about one transplant a day; we would like to be able to raise that number to about 1000 a day."

A useful breakthrough in the treatment of renal failure, he reported, is the development of an artificial kidney which uses a new type of mem-

brane. The membrane is much more permeable for molecules in the middle weight range and accomplishes a complete dialysis in one-half the time present equipment requires, "with reasonably good results."

The new membrane is made of polyacrylonitrile and Dr. Honnburger described its performance as "quite different," a possible solution to the twin problems of patient load and high cost that now plague the treatment.

Patients prefer it, of course, he said, because of the shorter time required. So far 12 patients have been treated on the new unit, and the first patient now had had two years with it.

At the Necker Hospital, the ever-present problem of graft rejection is being attacked from several different directions, the French nephrologist said.

Pain: a call to action.

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Group E patients: Do not use Percodan if you have a known or suspected allergy to oxycodone or aspirin. Do not use Percodan if you have a known or suspected allergy to oxycodone or aspirin. Do not use Percodan if you have a known or suspected allergy to oxycodone or aspirin.

Group F patients: Do not use Percodan if you have a known or suspected allergy to oxycodone or aspirin. Do not use Percodan if you have a known or suspected allergy to oxycodone or aspirin. Do not use Percodan if you have a known or suspected allergy to oxycodone or aspirin.

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Current Opinion

What's In A Word? OR Guilt By Definition Part II

By Dr. JONATHAN O. COLE

Psychiatrist, McLean Hospital, Belmont, Mass.,
and Lecturer in Psychiatry, Harvard Medical School;
excerpted from Massachusetts J. Mental Health, Winter, 1972.

LET'S TAKE REDEFINITION as an example for consideration of the ramifications. One behavior modification approach to bed-wetting is the use of an alarm system which is triggered when the patient urinates in bed. Activation of the loud alarm scares the subject and presumably conditions him not to wet the bed. This

sometimes works. Less drastic behavior modification techniques such as withholding liquids before bedtime and waking the subject up during the night to go to the bathroom may also help. Occasionally rare organic abnormalities are found which can be treated. In addition, certain drugs, particularly the tricyclic antidepressants, are clearly more effective than placebo in causing patients to stop wetting the bed. It is even possible that the bed-wetting is a symptom secondary to conflict within the family as a whole and it may well be that family therapy would be successful in some cases and that individual psychotherapy might be of use in others.

Clockwork Orange Analogy

I, too, have read *Clockwork Orange*. But I have no reason to believe that current methods of behavior modification or rehabilitation are anywhere near to being developable or implementable to be able to produce the result described in that scientific fiction novel. When

Acceptable to Patient?

The main issue in attempting to cure bed-wetting is to figure out a treatment which works and which is acceptable to the patient, and several might have to be tried. As with other forms of behavior modification, the question can be raised as to the informed consent of the subject.

It seems likely that most people, including children who wet the bed, would rather not wet the bed and are therefore willing to go along with any reasonable approach to treatment. Assuming there are some individuals, adults or children, who do not wish to stop wetting the bed, they presumably are unteachable. However, society, manifested perhaps by an angry mother, will at some point force the individual who wishes to continue wetting the bed to handle his own laundry, sheet changing, etc., invoking another form of behavior modification, namely aversive conditioning. It may or may not work, particularly if it is not systematically applied.

Attitude of Prisoner

In prisons where behavior modification programs have been tried, there must be parallels to the bed-wetting paradigm. Assuming a prisoner is clearly informed about the nature of a behavioral modification program and has the option to withdraw from it if he finds it unpleasant or undesirable, there seems to be no conceivable objection to offering a prisoner or a group of prisoners a chance to change behaviors which they agree need changing.

There must be some proportion of the class including all prisoners who feel that their behavior in the past has caused them to get into trouble repeatedly and who would welcome an opportunity to change themselves in such a way that they could stay out of trouble in the future. The impositions

on Social Welfare in Massachusetts which bans the study of psychotropic drugs in prisoners. The earlier draft of the bill sought to put severe limitations on the use of psychotropic drugs in prisoners.

Again, I think that the *Clockwork Orange* fantasy was operating in the minds of the proponents of the legislation. Psychotropic drugs are assumed to be, in some way, evil. The proponents may well suspect that some drugs are adding; other drugs probably change personality or in some way compromise the subject's mind or behavior.

Again, I would agree that some psychotropic drugs under some circumstances are not appropriate for use in prisoners and probably have been abused either by the prisoners or by those responsible for the prisoners.

Use in Prison

I understand that in the past there had been extensive prescribing of sedative and anti-anxiety drugs in Massachusetts prisons at the request of the prisoners. These drugs, which resemble barbiturates in their action, are liable to abuse and may well have been requested by the prisoners as a way of getting "high." Also, in other parts of the country, intramuscular injections of antipsychotic drugs are sometimes used in prisoners or juvenile delinquents in an attempt to suppress violent, hostile, assaultive behavior. I have recently testified in court against such use of chlorpromazine by a facility for juvenile delinquents in New York State. There, according to the records I have examined prepared by the facility's treatment staff, youths were often given intramuscular chlorpromazine after having a verbal argument with a counselor and becoming upset when placed in solitary confinement.

To my mind both kinds of psychotropic drug use described above constitute misuse. Antipsychotic agents are "nervikill" when used to punish inmates of correctional facilities for infractions of the rules. Further, when used to treat hostile, rebellious, assaultive behavior in prisoners, they are probably ineffective. On the other hand, they are excellent drugs for treating schizophrenic illnesses and are also effective in reducing impulsive unstable behavior in some patients with marked frequent mood swings. To control this type of psychopathology, low steady maintenance doses of the drug are necessary. Episodic intramuscular injections are not appropriate.

The Prisoner With Anxiety

Similarly, diazepam or chloridazepam or even the barbiturates are sometimes quite effective in treating both chronic and acute neurotic anxiety. When a prisoner is suffering from a clear anxiety state which cannot be adequately handled by either counseling or environmental manipulation, then such drugs are appropriate. Antidepressants may well have a place in the treatment of mild to moderate depression in prisoners. Lithium carbonate has been reported to be quite helpful in controlling severely disturbed, impulsive, assaultive behavior in prisoners identified as having such behavior with great frequency. Anticonvulsive medication may occasionally be

helpful in prisoners whose unstable, antisocial behavior may be secondary to abnormalities in brain function.

Lack of Studies

In short, I believe that psychotropic drug use in prisoners can occasionally be most appropriate either the physician or psychiatrist prescribing drugs for prisoners must be wary about the abuse potential of some of these drugs. Furthermore, there have been almost no systematic studies of the effectiveness of psychotropic drugs in treating various symptoms and behavioral adjustment problems in prisoners. Such research badly needs to be done.

Again, within any prison, I am sure there is a group of individuals who feel very uncomfortable within themselves and very unsure of their ability to maintain stability or well organized behavior either within the prison or later in the community. Such individuals often want help and it is possible that present or future drugs will be able to provide it. Some proportion of criminality is likely to be secondary to some type of abnormality in brain function or to the presence of intense emotions with which the patient's personality cannot cope.

Need for Research and Review

I am not arguing for the promiscuous testing of all sorts of new psychoactive drugs on defenseless prisoners. I am in favor of well designed, well planned and thoroughly reviewed research projects—the review must contain institutional review at the prison with prisoner participation—which result in the completion of sound research projects that provide meaningful information about the effects and usefulness of psychoactive drugs in prisoners. Such studies should be of benefit not only to the prisoners participating but ultimately to prisoners in general. In conclusion, I'd like to pray for sanity, restraint and judgment in both the use and the interpretation of the phrases "behavior modification" and

"... to kill off a treatment approach because someone somewhere sometime might conceivably be given it against his will or punitively is to do malicious harm to us all."

"psychotropic drugs." Neither the words nor the treatments denoted by them (justly or unjustly) are either necessarily bad or good. Please don't use these words as epithets. Both drugs and behavioral techniques can do a lot of good.

I am also pleading that treatments be evaluated on the basis of their efficacy and used if they work and condemned if they don't. They should be condemned also if they do more harm than good. But to kill off a treatment approach because someone somewhere sometime might conceivably be given it against his will or punitively is to do malicious harm to us all. Psychiatric treatments are not nearly effective enough now; to block off study or application of newer approaches is to condemn us all to treatment by whim or belief and to return us to a pre-scientific primitive level of psychiatric practice—and unevaluated practice at that!

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See facing page for Brief Summary

*See dosage and administration section of Brief Summary

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Dr. Warren Honored at Bunker Hill Ceremony

Continued from page 1

successful treatment of smallpox, he "acquired a high reputation among the faculty," according to *Harper's Encyclopedia of United States History*. In his practice, he relied primarily on the leeches, purgatives, cupping devices and herbs that then constituted the physician's armamentarium.

However, Dr. Warren's fame rests on his role as one of the prime organizers of the revolt against British rule through the committees of correspondence in each community.

He was a protégé of Samuel Adams, chief strategist of the colonists cause. At a meeting at Dr. Warren's house, in September, 1774, Samuel Adams, James Otis and others discussed the formulation of demands in a Boston town meeting that "forced the British government to prepare for war with Massachusetts," historians later said.

Aided by Doctor Brother

In all this Dr. Warren had the help and collaboration of his physician brother, Dr. John Warren, a participant in the Boston Tea Party. Dr. John Warren later drew up plans for Harvard Medical School, became its first professor of surgery and anatomy, and helped found the Massachusetts Medical Society.

In September, 1774, Dr. Joseph Warren personally drafted the coercive laws under which the British governor had closed the port of Boston and confiscated local taxes. This was a daring open challenge to British rule. It was, historians later said, "a complete declaration of war against Great Britain." And Dr. Warren, as soon as it was passed, handed a copy of it to Paul Revere who personally rode to Philadelphia to deliver it to the rebellious Continental Congress which adopted it after much debate.

Dr. Warren played a leading role in one of the pre-Revolutionary uprisings that he and Sam Adams kept churning up. On the occasion of the fifth anniversary of Boston Massacre, Dr. Warren delivered the annual oration. British officers filled the Old South



DR. JOSEPH WARREN

Meetinghouse expecting to "beat up a breeze," in Samuel Adams' phrase. But Adams welcomed them civilly and then Dr. Warren, clad in a "Ciceronian toga, mounted the black draped pulpit"—surrounded by the most violent of the revolutionaries, the Adamses, Coopers, John Hancock, and the Boston Select-

men. Dr. Warren concluded his oration without provoking a riot by carefully not using the words, "bloody massacre." But when he finished, Samuel Adams jumped up, praised and thanked Dr. Warren and proposed another oration for the following year "to commemorate the bloody massacre!"

Whereupon the British officers jumped up, crying "O Fie, O Fie," and waving their arms indignantly. At that moment a British regiment was passing by, its drums rolling. Some of the effeminate thought the British were crying "Fire!" and made for the doors but a great many more thought they were about to be slaughtered in a British trap—and they went out the windows.

Dr. Warren presided over the Massachusetts Provincial Congress in 1774 and chaired its committee of safety. He was commissioned a major general in the Massachusetts militia.

When Gen. Thomas Gage, the British governor, sent troops to arrest Samuel Adams and John Hancock and to destroy the military stores of the militia at Concord, Dr. Warren's friends informed him of the troop movements and he had previously arranged for Paul Revere to arouse the countryside. Dr. Warren has been credited by some authorities with organizing the Indian-style fighting that defeated the British troops at Lexington and Concord.



The 10-cent stamp commemorating the 200th anniversary of the Battle of Bunker Hill, issued on June 17, 1975. The design features the dying Dr. Warren. It is based on a detail of the famous painting by Trumbull on page 1.

Patient Role Urged In Antitumor Drug Use in Pregnancy

Medical Tribune Report

NEW ORLEANS—Let the patient participate in the decision as to whether antitumor drugs, which are highly teratogenic, are to be administered during pregnancy.

"This was the advice of Dr. Walter R. Cherry, director of post graduate education at the Good Samaritan Hospital, Phoenix, to physicians attending the New Orleans Graduate Medical Assembly.

"People with malignancies do get pregnant," he reminded. "We know that the risk factor of fetal abnormalities runs as high as 45 per cent to 50 per cent in some of the cancer drugs.

"The mother should be told this. She should know, and her wishes must be considered."

Dr. Cherry's own view is: "If you have to use it, do it." But if a drug is not essential to the pregnant patient's well-being, avoid it.

He noted that most of the common medications, including antibiotics, cold remedies, and antihistamines, have some teratogenic qualities. But physicians should not over-react and go to the extreme of withholding essential medicines. "Balance the risk," said Dr. Cherry. "If a drug is essential, it ought to be used."

At the same time he discouraged the prescription of drugs just because they are available.

"Take patient discomfort, vomiting. The condition is not life-threatening. In this circumstance, don't use antitumor drugs," the obstetrician advised. "And in mild infections, don't give antibiotics."

Regular Prescription of Iron

He added that the only chemical which should be prescribed regularly is the one the body needs but cannot store—iron. "A pregnant woman needs large amounts of iron. It is innocuous, except in gross overdoses."

There is a serious question, he said, as to whether a pregnant woman needs prescription vitamins.

He warned against a tendency to prescribe drugs "just to make the patient feel better."

Dr. Cherry advised aggressive measures against the development of toxemia.

He told the New Orleans Graduate Medical Assembly The condition—signs of which are rising blood pressure, excessive weight gain, puffiness of the face, eyes and fingers, kidney damage—is not an indication for immediate delivery, he said. "You don't have to subject the baby to immaturity."

Onset of toxemia "is an indication that the patient has lost her ability to cope with physiological stress."

"Be aggressive in guarding against the condition. Watch for elevating blood pressure, rapid weight gain, kidney damage, a special kind of swelling that is not just edema. Don't confuse puffiness of the face and fingers with the usual swelling of ankles and feet."

He said the best safeguard is to keep the patient in good health.

Arteriosclerotic Basis Denied For Bulk of Senile Dementia

Continued from page 1

to be "essentially identical" to presenile dementia of the Alzheimer type. He estimates that 65 per cent or more of all senile dementia patients have the Alzheimer form—and therefore thinks that therapy directed at treating blood flow problems is totally useless in this majority.

Another highly significant research finding, in his view, is the evidence that the brains of "normal" elderly people can show the same three lesions observed in senile dementia: nerve cell loss, neurofibrillary tangles composed of "twisted tubules," and senile plaques.

"Physically, the lesions are very much the same," Dr. Terry said. "In demented patients, they are exaggerated in number, but they are the same changes as those found to a much lesser extent in people who seemed to be functioning normally at the time of their death in the seventh or later decade."

Link to Psychometric Deficiency

Furthermore, the investigator pointed out that a close, positive correlation has been found by other research groups between concentrations of plaque in the cerebral cortex and the degree of psychometric deficiency shown by the patient.

Dr. Terry cautioned, however, that there is still no consensus as to whether the process that causes the rapid decline in mentation seen in dementia is the same process responsible for the "more or less steadily declining" or "variable rate" seen with advancing age and called "benign memory loss."

One process may be superimposed on the other, he said. And why the decline should be so "tragically severe and swift in some and marvelously slow in others cannot yet be explained."

Even the question of hereditary influence remains uncertain. There is some evidence, Dr. Terry observed, that "it helps to come from the right lineage" since the risk among first-order relatives of patients with senile dementia is significantly increased, and presenile dementia apparently occurs in some families with an autosomal dominant mode of inheritance. But most cases of senile dementia are sporadic, he said.

Sociologic Impact Stressed

Stressing the sociologic impact of senile dementia, Dr. Terry cited two statistics: nearly 11 per cent of the U.S. population over the age of 65 is said to have some degree of the disorder, and about 4.5 per cent of these elderly people are severely demented.

This is a "huge public health problem that has gone largely unrecognized," he said. Public health statistics are "grossly misleading" since senile dementia is not listed among 200-plus common causes of death and is almost never entered on death certificates yet "probably accounts directly or indirectly for some 120,000 deaths annually."

All three of the major brain lesions found in senile dementia are being

studied by Dr. Terry and co-investigators at Einstein.

To determine nerve cell loss, for example, they are now utilizing a new computerized and automated nerve cell counter. This equipment, they believe, promises to yield data far more efficiently and accurately than did previous "hand counts."

Research in their laboratory and elsewhere on the neurofibrillary tangles first shown that the fibrillary material first described by Alzheimer in 1906 is composed of "abnormal" twisted elements which average 22 nm. in outside diameter and narrow about every 80 nm., Dr. Terry said. These have been found to date only in the human brain—and only in the brains of the elderly or of patients with senile dementia or a few other pathologic conditions including postencephalitic Parkinsonism and Guam-Parkinsonism dementia.

Normal microtubules have a slightly wider diameter and are known to be made up almost entirely of tubulin, a protein consisting of an alpha-monomer (molecular weight 56,000) and beta-monomer (molecular weight 53,000).

Dr. Terry pointed out that since the normal microtubule or neurotubule resembles the twisted tubule in many respects, investigation is underway to determine whether the abnormal analog is a modification of normal tubulin or an entirely new protein.

May Be Neurofilaments

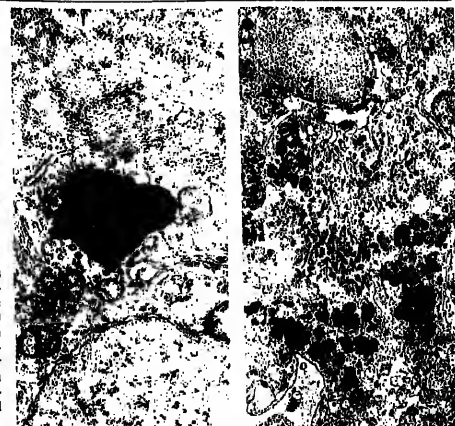
There is a "real possibility," he believes, that such twisted tubules are not neurotubules but rather a pair of helically wound neurofilaments. In its normal state, the neurofilament has a diameter of 10 nm., is ultrastructurally different from the neurotubule, and has in the human being a molecular weight of 53,000.

"If the twisted tubule is a modification of one or another of these proteins," he commented, "then we must look to the way in which it was modified. This might result from abnormal oxidation or perhaps by binding with a metal such as aluminum."

Experiments with certain animals have demonstrated that injection of aluminum into areas of the brain or spinal fluid will cause formation of neurofibrillary tangles as at autopsied water, Dr. Terry said. Also, he noted that some investigators have reported finding abnormally high aluminum concentrations in the brains of patients with the Alzheimer type of dementia.

Tracing the modification to oxidation would mean that antioxidants could be tried therapeutically, Dr. Terry continued. This might give support to treatment with such antioxidants as vitamin E. On the other hand, if modification is due to a metal it "would be logical" to try a chelating agent.

"But in either case," he said, "we would have some rationale for treatment instead of trying every compound on the shelf as is now often the practice. Too frequently, in fact, drugs are given without even making an assay."



Neurofibrillary tangles are evident in portion of neuron, left. Nucleus is at lower right, with micron marker; adjacent cytoplasm contains arganules plus single lipofuscin body. Neuritic plaque, right, shows irregular central core of amyloid surrounded by number of abnormal neurites.

meat of patients to determine whether they have senile dementia of the Alzheimer type or the less common form caused by arteriosclerosis."

The other possibility—that twisted tubules are a new protein—would mean that the cell has somehow obtained new genetic material, Dr. Terry noted.

One way this could happen would be through a virus, but in his opinion no virus has, at yet, been found that can be proved to play such a role. The other way is by depression of a gene that is present in many or all human beings but becomes depressed for some reason. Causes of depression would thus have to be studied, he said.

Analysis of twisted tubules has been difficult ("and expensive") but Dr. Terry's coworkers have now isolated the substance from postmortem brain specimens of patients with senile dementia and Guam-Parkinsonism dementia. Electrophoretic studies indicate that the dissolved twisted tubules migrate at rates indicating an approximate molecular weight of 50,000.

A Wholly New Protein?

"This might mean they are closely related to neurofilament, or that microtubule protein has lost a peptide or segment, or that this is a wholly new protein," he said. "The only way we can tell is by doing further analyses."

Currently, the research group is attempting immunohistochemical identification of the unique protein band they have observed. Although the band seems to correspond to the twisted tubules, it will now be necessary to prepare antibody to the protein, label the antibody, "and then make sure the label reacts with the microscopic lesions before we can be absolutely certain of what we are confident is true but haven't proved."

Another project is the making of peptide maps of normal (tubule) protein, normal neurofilament protein, and twisted tubule protein so that the three can be compared.

What about the senile plaques that are found in the brains of the normal elderly and young adults with Down's syndrome, and in significant numbers in the brains of patients with the Alzheimer type of dementia?

Dr. Terry noted that plaques have some overlap with the tangles. The axonal and dendritic endings that make up a plaque are filled to a greater or lesser extent with twisted tubules. The intervening axon does not contain them. These neurites also contain many lysosomes and mitochondria.

Another component of plaque is amyloid—a fact, said Dr. Terry, that "gives rise to all sorts of thoughts about immune processes," since some investigators believe that one type of amyloid is made up of fragments of light chains of immunoglobulin.

Some investigators also consider amyloid deposits to be the primary change that leads to cortical destruction, producing both the plaque and neurofibrillary tangles. Dr. Terry disagrees with this view, stating his hypothesis that the presence of degenerative neurites in the plaque precedes the amyloid deposits. But in any case, he emphasized, amyloid from the plaque must be isolated and its nature determined.

"Changes in the immune system of aging organisms are currently of considerable interest," he said. "Certain aspects of immune systems decline with age while others actually increase in the sense that autoantibodies are more prominent in aged than in younger organisms, whether animals or man. The whole problem of loss of neurons with aging, for example, may possibly be one of autoimmunization."

Several studies have already documented the presence in some aged animals and man of a circulating antibrain antibody, he commented. If this antibody is labeled and put in contact with brain, young or old, "it reacts with neurons, thus showing that this is where the antigen is."

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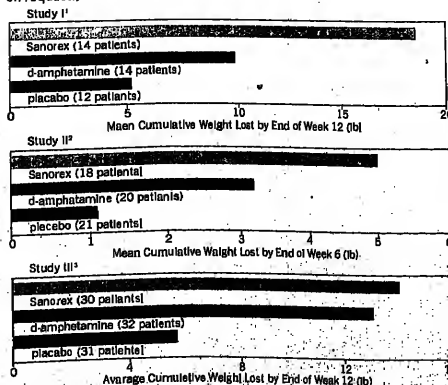
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Action of d-Amphetamine⁴

In animal studies, d-amphetamine (like food) activates afferent neurons leading to appetite centers in the hypothalamus. Resulting release of norepinephrine activates the receptor neurons. Unlike food, however, d-amphetamine also suppresses norepinephrine synthesis. Thus, increasingly larger doses of d-amphetamine become necessary to produce an effect.

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Simple one-a-day dosage is facilitated by 2-mg tablets (taken one hour before lunch). New flexibility (for the patient in whom 1 mg t.i.d. is preferred) is now facilitated by new 1-mg tablets (taken one hour before meals).

¹The significance of these differences for humans is uncertain.

For Brief Summary, please see facing page.

Wednesday, June 18, 1975

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Reference: 1. Problems and current concepts in the treatment of obesity. Scientific Exhibit presented at the New York State Academy of Family Medicine, New York, 1973. 2. Cohen, J. A. Cohen, L. A. Cohen, A. Double-blind clinical evaluation of mazindol, dextroamphetamine, and placebo in treatment of obesity. *Psychopharmacology* 34:356-366, July 1973. 3. Vermeil, J. Practical considerations for the management of obesity. In: *Obesity: Scientific Basis and Treatment*. American Medical Association, 1973. 4. *Obesity: Scientific Basis and Treatment*. American Medical Association, 1973.

Indications: In exogenous obesity, as a short-term (to four weeks) adjunct in a weight-reduction regimen based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors.

Contraindications: Glaucoma, hypersensitivity or idiosyncrasy to the drug, agitated states, history of drug abuse, during or within 14 days following administration of monoamine oxidase inhibitors (hypertensive crisis may result).

Warnings: Tolerance to many anorectic drugs may develop within a few weeks. If this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.

Drug Interactions: May decrease the hypotensive effect of antihypertensives; patients should be monitored accordingly. May markedly potentiate pressor effect of exogenous catecholamines. If a patient is recently taking mazindol must be given pressor amine agents (e.g., levatanol or isoproterenol) for shock (e.g., from a myocardial infarction), extreme care should be taken in monitoring blood pressure at frequent intervals and in giving pressor therapy with a low initial dose and careful titration.

Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related stimulants. Dependence has been extensively abused and can produce tolerance and severe psychological dependence. Manifestations of chronic dependence or withdrawal with mazindol have not been determined in humans. Absence of withdrawal has been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys. EEG studies and "liking" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been fully defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.

Usage in Pregnancy: In rats and rabbits an increased incidence of rib anomalies in rats was observed at relatively high doses. Although these studies have not indicated important adverse effects, the use of mazindol in pregnancy or in women who may become pregnant requires that potential benefit be weighed against possible hazard to mother and infant.

Usage in Children: Not recommended for use in children under 12 years of age.

Precautions: Insulin requirements in diabetes mellitus may be altered. Smallest amount of mazindol feasible should be prescribed or dispensed at one time to minimize possibility of overdose. Use cautiously in hypertension, with monitoring of blood pressure; not recommended in severe hypertension or in symptomatic cardiovascular disease including arrhythmias.

Adverse Reactions: Most commonly dry mouth, tachycardia, constipation, nervousness, and insomnia. Cardiovascular: Palpitation, tachycardia, dizziness, nervousness. Overstimulation, restlessness, nervousness, insomnia, dysphoria, tremor, headache, depression, irritability, weakness, gastrointestinal dryness of mouth, anorexia, taste, chemia, constipation, nausea, other gastrointestinal disturbances, skin rash, excessive sweating, chills, dizziness, impotence, changes in libido have rarely been observed. Eye: Long-term treatment with high doses in dogs resulted in some corneal opacities, reversible on cessation of medication; no such effect has been observed in humans.

Dosage and Administration: 1 mg three times daily, one hour before meals, or 2 mg per day taken one hour before lunch in a single dose.

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One Man...and Medicine

ARTHUR M. SACKLER, M.D.
International Publisher, Medical Tribune



For Arbitration in Malpractice Litigation

IT WAS a phone call for help.

"They are getting to be quite common these days. Emergencies appear to be escalating. This one was in reference to new legislation on malpractice insurance in the state of New York. The caller asked me to communicate with the Governor and members of the state legislature in opposition to the legislation. I knew of her reputation as a deeply concerned citizen; a fighter for rights of women, and a committed participant in consumer movements. There was no question as to her good faith. She is of the stuff that makes for good citizenship. Her name is Barbara Seamon, author of *Free and Female* and *The Doctor's Case Against the Pill*.

"Why are you so opposed to the new legislation?" I asked.

"Because it deprives patients, and particularly women, of protection they need."

"Do you have a specific case in mind that relates to women?"

"Yes, the example of women who develop vaginal cancer because of medication their mothers received during pregnancy."

"I have thought considerably about that," I said, "and it is precisely the sort of situation which would establish a precedent I don't believe you or I would like to see established. I am quite sure that you would not want laws passed with retroactive punishments which would put your people exposed unfairly to double jeopardy."

"That's true," she said.

"Well," I said, "there was a time when diethylstilbestrol was recognized as an effective treatment for spontaneous abortion. In fact, the generic advocates of the drug insisted it was more economical than progesterone which was also available. It was generally accepted that hormone therapy made possible what was miscarrying and was not treated with DES or progesterone could have claimed malpractice in a suit at that time. Today, on the basis of what you would like to see done, the physician who could have been subject to malpractice liability by his failure to treat the miscarrying women then could now be subject to malpractice liability because he *had* acted in accord with prior good practice."

"As to the relationship of diethylstilbestrol and vaginal cancer, obviously this is an issue that is emotionally charged. While some may say that the DES may be related to vaginal cancer, others could rightly hold that a woman may have a spontaneous abortion because of a defective fetus; that DES treatment salvaged the defective fetus; that the mother had a child she may have desperately wanted, but that the hypothetical inherent defect which 'nature' may have been rejecting made its appearance ultimately in a malignancy in a 'salvaged' child."

"Well," she said, "what do you be-

lieve we should do about this problem?"

"I can join you in supporting medication panels for malpractice cases."

"I think," she said, "that such panels should have consumer representation."

"Agreed. But that representation should be by individuals who would be truly objective and recognize they represent the interest of both the patient as an individual and a member of society. In any event, please send me the bill and the documents you have prepared so I can study them before acting..."

"Defensive" Medicine

The discussion was longer than the above and touched on some aspects which appear to be lost to many members of the public. I had mentioned to my caller the fact that malpractice liability suits and consumer pressures have been building up in such a way as to force physicians into "defensive" medical practice. The doctor is being increasingly confronted by an unfair dilemma of choices and placed in a "no win" situation.

He can, as was customary in prior times, use his diagnostic judgment and order only those tests which he believed were truly indicated, a minimum number of X-rays, avoid biopsies and hospitalization except for clearly defined indications. On the other hand, if he is sensitive to the manner in which malpractice liability judgments have been made, he can "cover all the bases" for his own safety, but at the patient's cost, both economically and physically. I would prefer to have a minimal amount of X-ray radiation diagnostically. She agreed.

I wonder how one can explain to people of good will and good intent that doctors, as a profession, do not want to deprive a patient of just compensation for medical accidents or negligence. The realities point to a dilemma: at the time of medicine's greatest achievements (decreasing infant mortality, increasing life expectancy, and the conquest of so many infectious and other diseases), the medical profession confronts its greatest liability in respect to malpractice. The greed of a minority of litigious patients and the self-interest of some trial lawyers in winning the largest possible settlements is creating an unfair situation for the majority of patients—those of good faith.

When a doctor's liability insurance threatens his practice, he has few choices. "Defensive" use of extensive diagnostic procedures is one; moving to a state or choosing a specialty where the

Medicine on Stamps

Jean Martin Charcot



Born in 1825, the son of a Paris coach builder, Charcot became the founder of modern neurology. He is best known for his work in arthritis, begun during his student days, but he also contributed to research on poliomyelitis, hysteria, epilepsy, cerebral function, multiple sclerosis, and locomotor ataxia. A talented artist and music lover, strongly resembling Napoleon in appearance, he was the most colorful teacher of medicine of his day.

Text: Dr. Joseph Kler
Stamp: Minikus Publications, Inc., New York

malpractice liability is less may be another. The physician certainly cannot be expected to subsidize medical care by taking money out of his life savings to either cover a liability suit or quadruple insurance premiums. Regardless of any of the above, there is one thing that is clear but not comprehended by those who oppose corrective measures to the present epidemic of liability suits—the cost of court judgments and insurance premiums must be ultimately paid by one group, patients themselves.

A National Need

Restraint of the escalating cost of health care services is a national need even as the sick are entitled to sound medical practice as well as fair economic protection for the unfortunate victims of either negligence or accident. Reason, if necessary through arbitration or mediation, is essential if malpractice liability insurance is not to become an ever-growing burden for the majority of patients, as well as physicians. The interests of doctors and most of their patients are in the last analysis the same.

EPICRAMS—Clinical and Otherwise

Doctors is all swabs.
Robert Louis Stevenson (1850-94)
Billy Borer



"How do you feel about acupuncture?"
© 1975, Medical Tribune, Inc.

Small Cerebral 'Pacemaker' Eases Pain in Madrid Trials

Medical Tribune World Service

MADRID—A miniaturized cerebral "pacemaker" has been employed here in clinical trials to relieve pain in a cancer patient and in an amputee suffering from phantom-limb distress.

In addition to analgesic uses, the device may also have broad application in brain research and in the treatment of epilepsy, according to its developers.

The apparatus was devised by a team at the Autonomous University of Madrid headed by Dr. José M. Rodríguez Delgado, formerly of Yale. It consists of a plastic-coated disk containing integrated circuits and components, 40 mm. in diameter by 15 mm.

thick, implanted under the scalp, with six electrodes reaching into selected brain sites.

The coin-size pacemaker operates without batteries or external wiring. It receives power from radio waves that are picked up by a small portable transformer carried by the patient, allowing for two-way flow between the brain and a computer or control panel. The brain may be monitored in bipolar recordings, while stimulation



DR. DELGADO

in bipolar recordings, while stimulation



A subject equipped with an earlier, bulkier version of the brain stimulator developed by Dr. José M. Rodríguez Delgado's Madrid team.

Natural distinction

Wholesome and unadorned young beauty impresses the eye with its natural distinction. Among medicinalals, such natural distinction will be found in SENOKOT Tablets/Granules.

Standardized senna concentrate has two claims to natural distinction. In SENOKOT Tablets/Granules, it is standardized for uniform action. And it is prepared from the de-seeded pod of *Cassia acutifolia*, discarding the leaves that contain coarse resins.

Virtually color specific, SENOKOT Tablets/Granules provide gentle, predictable overnight action, usually without side effects or recommended dosage levels. As regularity returns, laxative dosage can be reduced gradually or eventually discontinued.

Further research



Senokot
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may be provided to induce or restrain electrical activity.

According to Dr. Delgado, the pacemaker constitutes no improvement over "first generation" models that he used in the treatment of pain, thanks to its reduced size and freedom from encumbering wires. It also avoids the discomfort and possible infection resulting from sockets and leads piercing the scalp.

In treatment of the patient with plantations limb, programmed stimulation of the septum led to relief of previously intractable pain and diminished the patient's hostility. While final evaluation will require long-term follow-up, this case has demonstrated to the Delgado team the feasibility of transdermal, remotely controlled, programmed stimulation of the human brain for therapeutic purposes.

Regarding the possibility of treatment of epileptics, Dr. Delgado theorizes that a pacemaker-radio system may be devised in conjunction with a portable computer and power source that would continuously monitor brain activity and supply preventive stimulation when an attack was imminent.

Quadriceps Surgery In Children Simplified

Medical Tribune World Service

KYOTO, JAPAN—Over the past eight years, diminution of the quadriceps due to thigh injections during infancy has been cured with "relatively simple surgery" in 50 patients aged five to 12, at the Nishitaga National Sanatorium.

According to surgeons there, the operation involves cutting out the affected muscle and separating muscle adhesions.

Conventional surgery had called for excising the tendon besides removing the affected muscle, the surgeons told the *Japan Times*. Moreover, the psychological impact of the new treatment, which leaves only one scar, is less for young patients, they said.

"Postsurgery surveys revealed that all the cases have nearly regained full capacity to walk," the report from the sanatorium revealed. Citing the case of an 11-year-old girl operated on eight years ago, the Japanese surgeons said that before the operation, she could bend her knees only 30 degrees, but now she can bend 130 degrees and walk without difficulty.

Wednesday, June 18, 1975

Tribune Economic Analysis



New York's troubled financial terrain has long been ready for a political bombshell. The shrewd speaker of the lower house of New York legislature, Stanley Steingut, has just exploded it. He has enlisted the advice of the always formidable Ralph Nader, and he has found a model for New York State to follow in all of places, the populist state of North Dakota.

It's a far cry from the plains of Bismarck to the canyons of Wall Street. Nevertheless, New York, banker to the world and therefore busted, is taking as its model the "operation bootstrap" that the farmers of North Dakota devised during the farm depression of the otherwise prosperous 1920s. The Bank of North Dakota is the only state-owned bank in the country, and it operates at a profit. Its president, H. L. Thorndal, testified at the hearing called by Speaker Steingut that this unique institution, founded with a \$2 million investment, has earned a cumulative profit of \$83 million in the 56 years of its existence. Last year alone, Mr. Thorndal stated, the Bank of North Dakota reported \$16 million of profit to the state legislature.

Nader invited New York State to follow where North Dakota has led. Speaker Steingut's staff advisors discovered that their original guesstimate that the state, though busted, has a deposit float of \$3 billion in banks throughout the state ready for redeployment on the North Dakota model is low. Speaker Steingut also asked me to furnish a recommendation for this emergency, and I will summarize it in this space next week.

Do you think there is any real possibility that New York City's credit problems could be solved by selling small bonds to people through the Off-Track Betting Offices? My patients believe this will happen.

New York Physician

I don't. Average people—even betting folk—tend to be smarter than banks. If even banks don't want to be stuck with any more NYC garbage, why should people?

Can mortgage rates be expected to go down? I should like to build a vacation home in New England, but the mortgage rates I'm quoted make it ridiculous.

Boston Physician

I fear mortgage rates are headed up again. Their high level is only one reason why you're right in regarding building costs as ridiculous. Because you're right, buying makes better sense than building.

Eliot Janeway regularly answers MEDICAL TRIBUNE readers' questions.

MEDICAL TRIBUNE

19

Aerosol Sniffers 'Playing Russian Roulette'

Medical Tribune Report

NEW ORLEANS—Teenage spray can propellant sniffers are playing Russian roulette and ought to be so informed.

Dr. Leo G. Horan, chairman of the health services center at the University of Louisville, made these observations to physicians attending the New Orleans Graduate Medical Assembly.

But, he said, concentrations of the fluorocarbons—Freon 11 and Freon 12—are far below the single exposure lethal level in beauty salons where hair preparations are applied, and even lower in the bathrooms and kitchens of homes, in which an average of 15 spray cans can be found.

Dr. Horan estimated that 100 youths now die every year as the result of sniffing concentrations of nearly 100

percent of the propellants from bags or balloons. The death rate has declined from the peak years because there is a trend away from drug addiction and toward the use of alcohol.

Route to Drug Addiction

Dr. Horan said sniffing is a route toward drug or alcohol addiction. "It is essential that young people know the hazards," he added. They should be informed in the homes and at Boy Scout meetings that they are playing Russian roulette.

He said eventually it may be necessary to ask manufacturers to lessen the amount of Freon 11 in spray can mixtures.

The interstat said animal experimen-

tion has demonstrated that nothing happens when concentrations of up to 150,000 parts per million—or 15 percent—of Freon 11 are inhaled. Between 15 percent and 20 percent results vary, but when the concentration is above 21 percent death is inevitable.

On the other hand, concentrations of as much as 95 percent of Freon 12 are not deadly, he said.

A study in beauty salons showed that the maximum concentration around the head of an operator who is applying hair spray is 250 to 310 ppm. In a closed bathroom, the greatest concentration is 50 ppm.

Dr. Horan noted that the fluorocarbon propellants are similar to halothane.

INJECTABLE



Injection DECADRON® Phosphate (Dexamethasone Sodium Phosphate) (MSD) equivalent to 4 mg dexamethasone phosphate per ml, in 1-ml, 5-ml and 10-ml disposable syringes and 1-ml, 5-ml, and 10-ml vials.

INGESTIBLE



Tablets DECADRON® (Dexamethasone) (MSD) 0.75 mg. in 100 and 500 tablets (package of 12).

BREATHABLE



RESPHALER® DECADRON® Phosphate (Dexamethasone Sodium Phosphate) (MSD) containing per metered spray, dexamethasone sodium phosphate equivalent to approximately 0.1 mg dexamethasone or 0.084 mg dexamethasone, fluorocarbon propellants and alcohol 2%, in 12.5 g cartridge delivering at least 170 sprays and refill cartridge.

DROPPABLE



Sterile Ophthalmic Solution DECADRON® Phosphate (Dexamethasone Sodium Phosphate) (MSD) 0.1% equivalent to 1 mg dexamethasone phosphate per ml, in 5-ml Ophthalmic ALPHALIC DISPENSER and 2.5-ml and 5-ml dropper bottles.

SPREADABLE



Topical Cream DECADRON® Phosphate (Dexamethasone Sodium Phosphate) (MSD) 0.1% equivalent to 1 mg dexamethasone phosphate per gram, in 15-g and 30-g tubes.

SPRAYABLE



Topical Aerosol DECASPRAY® (Dexamethasone) (MSD) 10 mg per 30-g container, TURBINARE® DECADRON® Phosphate (Dexamethasone Sodium Phosphate) (MSD) equivalent to approximately 0.1 mg dexamethasone phosphate or 0.084 mg dexamethasone per metered spray, in 12.5 g cartridge delivering 170 sprays.

DECADRON®
(DEXAMETHASONE) (MSD)

Now Suspension
DECADRON-LA®
(DEXAMETHASONE ACETATE) (MSD)
equivalent to 6 mg dexamethasone per ml, in 5-ml vials.

"Let me tell you about the medicine I'm going to prescribe."

TALKING OVER VALIUM®(diazepam) THERAPY WITH YOUR ANXIOUS PATIENT



A patient often benefits by a greater understanding of his treatment program. You may find it helpful to make your patient aware that the purpose of therapy with Valium is to help reduce discomforting and disabling symptoms of excessive psychic tension and anxiety. It is beneficial for him to understand that much of his tension and anxiety can be relieved by your reassurance and counseling, and that these measures can do more than anything else to help him cope with his basic problems. The patient is reassured in knowing he can expect his medication to help him avoid feeling overwhelmed by his symptoms.

And it's also good for him to realize that he will be taking Valium only as long as he needs it.

Your expressed confidence in the medication prescribed, and the positive atmosphere in which therapy is given and accepted, work to the patient's advantage.

Selection of a dosage regimen is an important consideration when Valium (diazepam) is prescribed, and dosage should be individualized to achieve maximum beneficial effect. If the patient understands clearly when and how much to take, and if he knows why it's to his benefit to follow the regimen closely, the chances are better that he will take the medication precisely as directed. That should help avoid missed doses and discourage taking too much or too little medication — all of which can have an undesirable effect on the management of the patient's condition.

*"It's important that you
follow my directions
closely."*

*"I'll see you again the week
after next and we'll see
how you're making out."*

Your patient is often likely to feel reassured when you talk about seeing him again to check his progress. A planned visit evidences your continued interest and affords the patient an opportunity to report improvement he has made and to relate whatever continuing or additional difficulties he may be experiencing. It's also a chance for him to describe his response to therapy with Valium.

During follow-up visits, as your patient talks about his medication and about its effects on his symptoms, he will provide the kind of information that will be of great help in evaluating total therapy, adjusting the dosage of Valium, or discontinuing the medication entirely if that seems indicated.

Valium® (diazepam)

2-mg, 5-mg, 10-mg scored tablets
for individualized treatment of psychic tension



Please see the following page for a summary of product information.



Valium® (diazepam)

2-mg, 5-mg, 10-mg scored tablets

Prompt, effective action. Valium (diazepam) works rapidly to relieve pronounced psychic tension in patients overreacting to stress and in psychoneurotic patients.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other anti-

depressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Dosage flexibility. Scored Valium 2-, 5-, and 10-mg tablets give you dosage flexibility no tranquilizer capsule can match.

depressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice, periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-B-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Wednesday, June 18, 1975

Clinical Trials



Female Lag in Performance 'Not Due to Inherent Ability'

Medical Tribune Report

SAN FRANCISCO—The performance and physiological differences noted between male and female athletes may be socially and culturally induced and have little to do with physical differences, a physician-coach said here at a sports-medicine seminar.

His studies suggest that the big differences found between trained men and women are "not due to inherent ability," said Dr. C. Harrison Brown, director of student health services at California State College at Hayward.

For instance, he reported, young girls increased their oxygen uptake by about 25 per cent after six weeks of training—which was "as good as if not better than in boys." The girls showed normal growth and no sign of any changes that might be harmful, he noted.

Comparisons also showed that the maximum oxygen uptake of trained women athletes compared well with that of college distance runners despite the big differences among the untrained, Dr. Brown said.

With regard to excess adipose tissue—about 25 per cent in untrained high-school and college girls, compared with 14 to 15 per cent in untrained men—he found that the female distance runner has about half as much adipose tissue as her sedentary counterpart. During altitude training for the 1968

Olympics, adipose tissue was 8 to 9 per cent of body weight for the women, quite comparable to what is found in male athletes, he said.

Dr. Brown also observed that the trained adult woman, although she perspires less, appears to regulate body temperature as well as a trained adult man, and that women's muscles can show significant gain in strength through weight training without the same muscle hypertrophy found in men.

He cited a strength increase of 45 per cent with an increase in the lean muscle mass of the arms of only 1-2 per cent and of the legs of 4-5 per cent.

"This difference between the sexes is probably hormonal," he said.

The seminar was cosponsored by the American Academy of Podiatric Sports Medicine and the California College of Podiatric Medicine.

Fetal Pancreatic Protein

Medical Tribune World Service

KYOTO, JAPAN—A test of blood and pancreatic fluid samples taken from pancreas cancer patients has indicated the presence of a fetal pancreatic protein that may prove useful in the early detection of cancer of this type, Dr. Tatsuji Hatake, of Shinshu University, told a meeting of the Gastroenterological Society of Japan here.

Dr. Hatake and his colleagues used the pancreases of aborted fetuses to test for the protein in cancer patients. Eleven out of 13 blood samples and three of five pancreatic juice samples from cancer patients developed a reaction that indicated the presence of the fetal protein, he reported.

DENVER—Recent evidence suggests that some families are susceptible to groups of apparently unrelated cancers, Dr. Joseph R. Fraumeni, associate director of the Epidemiology Branch of the National Cancer Institute, said here.

Healthy members of such families may deserve increased medical surveillance if they presort with subclinical abnormalities, he told the National Conference on Advances in Cancer Management here, sponsored by N.C.I. and the American Cancer Society.

Over the past three years, Dr. Fraumeni said, studies carried out at N.C.I., Anderson University, and M. D. Crofton Cancer Center, Houston, have turned up about 75 families with genetic defects that appear to transmit a disposition to more than one form of cancer. For example, some families seem to be prone to both leukemia and breast cancer, others to cancer of the brain and the adrenals, and others to cancer of the colon and the endometrium.

Other recent epidemiologic surveys

strengthen the notion that some families are prone to cancers of the same site, he continued. The risk among close relatives has been found to be about threefold for most adult cancers, including carcinomas of the breast, stomach, colon, endometrium, prostate, and lung, he said.

The N.C.I. epidemiologist also noted that several forms of cancer occur in a higher than normal rate in patients with various genetic abnormalities—leukemia for example, showing an excessive incidence in patients with Bloom's syndrome and Fanconi's anemia.

Although environmental factors may play a role in familial cancer, Dr. Fraumeni said, he believes the overriding influence is genetic.

"Supporting this possibility," he said, "is the observation that the neoplasm that occurs either in familial aggregation or in genetic syndromes tends to develop at an earlier age than do nonfamilial occurrences of the same tumor and tends to arise multicentrically in the same organ or bilaterally in paired organs."

Artificial Elbow

Four patients suffering severe pain and inability to move their elbows have undergone total elbow replacement at University Hospitals in Cleveland. The artificial elbow is a hinge joint made of Vitallium and bonded to bone by methylmethacrylate. Dr. Kingsbury Helpe and Dr. Victor Goldberg, the surgeons, report functional mobility and absence of pain in all cases.

IMMATERIA MEDICA

Did You Say Work?

Work Is Dangerous to Your Health is the title of a book that turns out to be a handbook on health hazards of an occupational type—and not one selling laziness. We were so disappointed we looked in the opening pages and learned this title was developed in 1947 by the senior author, Jeanne M. Stellman, Ph.D. Her coauthor is Dr. Susan M. Daum, a physician concerned with occupational health. Looking further, we found an astonishing coverage of such diseases as well as a listing of the hazards of pipettors, herbicide makers, fishermen, glue makers, rubber vulcanizers—even physicians, nurses and scientific workers.

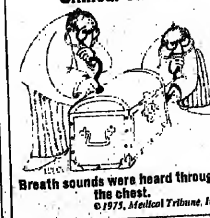
Yet not a word about showgirls, musicians, nightclub comics, Presidents, golfers, surfers, sunbathers, Midwestern School Deans, state hospital superintendents, businessmen, bosses, partners, editors, wives—the people who count.

The Hot Golf Ball

Goodrich Products, Inc., asserting that a hot golf ball will soar 20 per cent farther than a cold one, has marketed a compact portable heater which fires up three balls at once. What's more, Goodrich claims that once heated, the balls retain their soar power throughout the game. The heat reportedly increases its compressibility and resiliency so that it spins faster, increasing its projection.

We always thought our trouble was our swing. What a relief to know it's just those half-baked balls.

Clinical Cliché



Breath sounds were heard through the chest.
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